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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,356	05/03/2001	Donald Morris	032775-041	6890

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,356	MORRIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,19 and 25-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18, 19 and 25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Claims 18, 19 and 25-37 are pending.

Claim 1-17 and 20-24 have been cancelled.

Claims 18 and 19 have been amended.

Claims 25-37 have been added.

Claims 18, 19 and 25-37 have been examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-16 and 20 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 102

4. The rejection of claims 1, 5-9, 11-13 and 17 under 35 U.S.C. 102(b) as being anticipated by Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) is withdrawn in light of the cancellation of the claims.

5. The rejection of claims 1, 5-9 and 11-13 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference) as evidenced by Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS Reference) is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-7, 9-13 and 17 under 35 U.S.C. 103(a) as being unpatentable over Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) or U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference), in view of U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference) is withdrawn in light of the cancellation of the claims.

7. The rejection of claims 1, 5-9, 11-13, 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference) or U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference), in view of U.S. Patent number 5,840,502 (issued November 24, 1998) is withdrawn in light of the cancellation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

8. Claims 18, 25, 27-31 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS

reference), in view of Freshney (Culture of Animal Cells: A Manual of Basic Technique, second edition, New York, NY, 1987). Coffey teaches a method of oncolysis of a cellular composition consisting of ras-transformed C3H-10T1/2 fibroblast tumors mediated by intratumoral injections of reovirus serotype 3 (strain Dearing), see page 1333, bridging paragraph of columns 2 and 3; page 1334, Figure 4B. Initially the tumors were formed in syngeneic immune-competent C3H mice and then they were implanted as a tumor allograft into C3H mice at sites overlying the left hind flank.

Coffey also teaches a method of oncolysis of a ras-mediated human brain glioblastoma cell line, U-87 tumor implanted into the hind flank of SCID mice, see bridging paragraph of pages 1332 and 1333. Coffey notes that "...the human glioblastoma U87 cell line overexpresses the PDGFR and thus has increased levels of activated Ras", hence the Examiner regards the formed tumor as a ras-mediated neoplasm, see page 1332, column 3, paragraph 2. Treatment with the Dearing strain of reovirus serotype 3 resulted in "[n]ecrosis of tumor cells was due to direct lysis by the virus...".

Coffey does not teach the selection of a cellular composition for autologous transplantation, nor the step of freezing and storing the reovirus-treated composition in a solution containing dimethyl sulfoxide (DMSO). However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a cellular composition contacted with a oncolytic reovirus for autologous transplantation because clearly the syngeneic transplantation was effective in tumor regression and increased morbidity. One of ordinary skill in the art would have

been motivated to do so with a reasonable expectation of success by teachings in the Coffey article that (1) "[t]he selective replication of reovirus in cells with an activated replication of reovirus in cells with an activated Ras signaling pathway, coupled with the relatively nonpathogenic nature of [the] virus in humans...makes it attractive as a potential oncolytic agent and (2) "[t]he results from the C3H mouse model...suggest the feasibility of using this treatment in humans", see page 1332, column 3, last sentence of bridging paragraph and page 1334, column 1, last sentence, respectively. These observations support the use of a cellular composition for autologous transplantation in light of the successful syngeneic transplantation process.

Furthermore, Freshney teaches the storage of a "seed stock" in helping to ensure it remains free of contamination and readily available. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a oncolytic viral composition in a solution containing DMSO and preserving a "seed stock". One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings of Freshney that cryopreserving "seed stock" is a general practice implemented in cell biology to make certain there is continued availability of the selected stock.

9. Claims 18, 25-29 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference), in view of U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference). Coffey teaches a method of oncolysis of a cellular composition consisting of

ras-transformed C3H-10T1/2 fibroblast tumors mediated by intratumoral injections of reovirus serotype 3 (strain Dearing), see page 1333, bridging paragraph of columns 2 and 3; page 1334, Figure 4B. Initially the tumors were formed in syngeneic immune-competent C3H mice and then they were implanted as a tumor allograft into C3H mice at sites overlying the left hind flank.

Coffey also teaches a method of oncolysis of a ras-mediated human brain glioblastoma cell line, U-87 tumor implanted into the hind flank of SCID mice, see bridging paragraph of pages 1332 and 1333. Coffey notes that "...the human glioblastoma U87 cell line overexpresses the PDGFR and thus has increased levels of activated Ras", hence the Examiner regards the formed tumor as a ras-mediated neoplasm, see page 1332, column 3, paragraph 2. Treatment with the Dearing strain of reovirus serotype

Coffey does not teach the selection of a cellular composition for autologous transplantation, wherein the reovirus that contacted the said composition is an avian reovirus . However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a cellular composition contacted with a oncolytic reovirus for autologous transplantation because clearly the syngeneic transplantation was effective in tumor regression and increased morbidity. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the Coffey article that (1) "[t]he selective replication of reovirus in cells with an activated replication of reovirus in cells with an activated Ras signaling pathway, coupled with the relatively nonpathogenic nature of

[the] virus in humans...makes it attractive as a potential oncolytic agent and (2) "[t]he results from the C3H mouse model...suggest the feasibility of using this treatment in humans", see page 1332, column 3, last sentence of bridging paragraph and page 1334, column 1, last sentence, respectively. These observations support the use of a cellular composition for autologous transplantation in light of the successful syngeneic transplantation process.

Furthermore, U.S. patent #6,136,307 teaches that a variety of solid neoplasms and hematopoietic neoplasms can be treated and non-human mammalian reoviruses such as an avian reovirus can be used, see abstract; column 6, lines 45-51; bridging paragraph of columns 7 and 8; column 8, lines 19-32. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat both solid (i.e. liver, lung, pancreatic islet cells) and hematopoietic neoplasms (i.e. whole blood), as well as use an avian reovirus to mediate oncolysis. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the patent that suggests that either solid neoplasms or malignant tumors can be treated alternatively with an avian reovirus, see column 6, lines 37-51; bridging paragraph of columns 7 and 8; column 8, lines 42-56.

10. Claims 18, 19 and 25-37 are rejected under 35 U.S.C. 103(a) as being unpatentable Coffey et al. (Science 282: 1332-1334, November 13, 1998/ IDS reference), in view of U.S. Patent number 5,861,159 (January 19, 1999), Freshney (Culture of Animal Cells: A Manual of Basic Technique, second edition, New York, NY,

1987) and U.S. Patent number 6,136,307 (filed February 24, 1999/ IDS reference). Coffey teaches a method of oncolysis of a cellular composition consisting of ras-transformed C3H-10T1/2 fibroblast tumors mediated by intratumoral injections of reovirus serotype 3 (strain Dearing), see page 1333, bridging paragraph of columns 2 and 3; page 1334, Figure 4B. Initially the tumors were formed in syngeneic immune-competent C3H mice and then they were implanted as a tumor allograft into C3H mice at sites overlying the left hind flank.

Coffey also teaches a method of oncolysis of a ras-mediated human brain glioblastoma cell line, U-87 tumor implanted into the hind flank of SCID mice, see bridging paragraph of pages 1332 and 1333. Coffey notes that "...the human glioblastoma U87 cell line overexpresses the PDGFR and thus has increased levels of activated Ras", hence the Examiner regards the formed tumor as a ras-mediated neoplasm, see page 1332, column 3, paragraph 2. Treatment with the Dearing strain of reovirus serotype

Coffey does not teach the selection of a cellular composition for autologous transplantation contacted with an avian reovirus, nor the step of freezing and storing the reovirus-treated composition in a solution containing dimethyl sulfoxide (DMSO). However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a cellular composition contacted with a oncolytic reovirus for autologous transplantation because clearly the syngeneic transplantation was effective in tumor regression and increased morbidity. One of ordinary skill in the art would have been motivated to do so with a reasonable

expectation of success by teachings in the Coffey article that (1) "[t]he selective replication of reovirus in cells with an activated replication of reovirus in cells with an activated Ras signaling pathway, coupled with the relatively nonpathogenic nature of [the] virus in humans...makes it attractive as a potential oncolytic agent and (2) "[t]he results from the C3H mouse model...suggest the feasibility of using this treatment in humans", see page 1332, column 3, last sentence of bridging paragraph and page 1334, column 1, last sentence, respectively. These observations support the use of a cellular composition for autologous transplantation in light of the successful syngeneic transplantation process.

Furthermore, U.S. Patent #5,861,159 teaches a method of stimulating a systemic immune response to a tumor cell by administering a sustained release of therapeutic compounds to allow a host immune system to ameliorate local as well as metastatic tumors in a host. The immunopotentiating agent may be a cytokine such as tumor necrosis factor, GM-CSF, interleukin or interferon, see abstract and column 3, Summary of the Invention section. Immune system stimulating agents taught in the said patent would be effective in preventing tumor growth, tumor metastasis and tumor regression in a subject. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to implement the teachings of Coffey and U.S. Patent #5,861,159 in the method of preparing a cellular composition including immune system stimulating agents for autologous transplantation in order to destroy the neoplastic cells. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art the

manufacture of anti-tumor medicaments incorporating anti-cancer agents is efficacious for the in vivo treatment of cancer and the potentiation of a subjects' immune response.

Additionally, U.S. patent #6,136,307 teaches that a variety of solid neoplasms and hematopoietic neoplasms can be treated and non-human mammalian reoviruses such as an avian reovirus can be used, see abstract; column 6, lines 45-51; bridging paragraph of columns 7 and 8; column 8, lines 19-32. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat both solid (i.e. liver, lung, pancreatic islet cells) and hematopoietic neoplasms (i.e. whole blood), as well as use an avian reovirus to mediate oncolysis. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the patent that suggests that either solid neoplasms or malignant tumors can be treated alternatively with an avian reovirus, see column 6, lines 37-51; bridging paragraph of columns 7 and 8; column 8, lines 42-56.

Moreover, Freshney teaches the storage of a "seed stock" in helping to ensure it remains free of contamination and readily available. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a oncolytic viral composition in a solution containing DMSO and preserving a "seed stock". One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings of Freshney that cryopreserving "seed stock" is a general practice in cell biology to make certain there is continued availability of the selected stock.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
22 September 2003